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The Pulmonary Manifestations of Hodgkin's Disease

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PULMONARY MANIFESTATIONS OF HODGKIN'S DISEASE

A. INTRODUCTION:

Hodgkin's Disease is generally known to manifest itself in every organ, but the primary site is usually the lymphatic tissue. The disease frequently is confined to the lymphatic system either locally with recurrences or generalized, and how this latter process occurs is still disputed. It is speculated that there is spread via the lymphatics to other lymph nodes and/or hematogenously to distant organs; however, the possibility of a multicentric origin has not been entirely ruled out. Aside from the externally palpable nodes, the mediastinal and abdominal lymph nodes, and spleen are most frequently involved; somewhat less common sites are the skeletal system, liver, musculature and stomach. It is relatively rare in the intestines. In spite of the wide spread dissemination Hodgkin's Disease may paradoxically remain clinically quiescent for a long period of time (7,38). Although pulmonary manifestations are not uncommon they have not received sufficient emphasis in the literature. Involvement of the lower respiratory tract, i.e. trachea, bronchial tree, lung parenchyma and pleura are significant not only their inherent difficulty as a diagnostic problem to the clinician, but also because of its "life-threatening" potential to the patient. The purpose of this paper is to emphasize the importance of pulmonary Hodgkin's Disease as well as provide a brief classification related to X-Ray interpretation of pulmonary Hodgkin's Disease.

B. INCIDENCE:

Statistics on the frequency of the respiratory involvement yield wide variations. Ratkoczy, (25) an authority on the clinical manifestations, Roentgen diagnosis and therapy of Hodgkin's found pulmonary lesions in 17% of his cases.

In the following table according to Scheinmel, (29) statistics of parenchymal involvement are shown.

TABLE I	HODGKIN'S DISEASE CASES	LUNG PARENCHYMA INVOLVEMENT PERCENT
Castex, et al	340	4
Goldman, et al	317	8
Jackson and Parker	170	14
Perrier	273	26
Wolpaw	55	40

There are, concomittantly, divided views as to whether the respiratory system is involved in early or late stages of the disease.

C. ETIOLOGY:

The etiology of Hodgkin's Disease is still unknown. Many authors consider it as a neoplasm because of its invasive growth, destructive properties as well as it response to radiation therapy and invariably a fatal course. Because of the similarily of the granulomatous architecture with those produced by certain bacteria and/or viruses, some research workers still seek an infectious agent (6,14). Other authorities believe Hodgkins to be an usual form of chronic inflammation basically resembling a lymphoma which eventually undergoes malignant transformation (16). Clinically in the early stages of the disease, Hodgkin's simulates an infectious process and thus gives some credence to early investigators bacterial theory. In most cases, however, Hodgkin's Disease behaves and reacts to radiation therapy as radiosensitive tumors do (1). There is a close relationship between Hodgkin's Disease and other lymphatic tumors with strong histological evidence of transformation. On the basis of this observation Custer (9,10) and others (4,8,13,15,23,27) have classified Hodgkin's Disease as a malignant lymphoma.

D. PATHOGENESIS:

Hodgkin's Disease may be seen in any tissue containing a collection of lymphocytes or reticulum cells. Aggregates of lymphoid tissue are frequently evident in the bronchial wall and its supporting connective tissue. Lymphatic elements are also noted in the adventitial tissue surrounding the blood vessels, and between these vessels and neighboring alveoli (26). The pleura, similarly, usually contains small aggregates of lymphoid tissue. Therefore, pulmonary involvement may originate within the framework of the reticulum cells of the lung and from pre-existing lymphocytes or those lymphocytes from the systemic circulation (14,19). Lesions of Hodgkin's Disease develop not infrequently in the interstitial lymphatic tissue of the lung, per-se, or may spread from hilar and perihilar nodes into the lung parenchyma. Occasionally, the mediastinum, ribs, sternum or soft tissue of the thorax wall may give rise to hematogeneous or contiguous spread (25,27).

E. CLASSIFICATION OF HODGKIN'S DISEASE ACCORDING TO PATHOLOGIC ANATOMIC CHANGES:

Involvement of the lower respiratory system may be characterized by Pathological-Anatomical alterations which may serve as a useful tool to correlate the radiographic changes. This classification comprises three main groups according to the anatomical involvement with associated Roentgenological changes. Though each division is somewhat specific as noted below, it does not imply that some degree of overlapping does not occur over extended periods of time. In light of this flexibility an individual case may be incorporated within all three

divisions. This classification enables one to survey and classify pulmonary Hodgkin's Disease without necessarily implying that it manifests itself in one form exclusively.

I. COMPRESSION OF BRONCHI BY LYMPH NODES:

a). Disturbance in ventilation due to a check-valve mechanism of the segment supplied by the bronchus involved, resulting in obstructive emphysema.
b). Stenosis of the bronchus with atelectasis, and/or atelectatic-like pneumonia.
c). Blockage resulting in inspissation of secretions which eventually lead to tissue necrosis and abscess formation or gangrene.

II. INFILTRATIVE GROWTH FROM THE MEDIASTINUM TO THE TRACHEA, BRONCHIAL TREE AND LUNG PARENCHYMA:

a). Invasion of the trachea (clinically characterized by inspiratory stridor, non-productive cough, dyspnea, etc).
b). Invasion of bronchi with disturbances in ventilation with possible perforation and fistula formation.
c). Infiltrative growth from mediastinum into the lung parenchyma (Case 1).

III. HEMATOGENOUS OR LYMPHOGENOUS SPREAD:

a). Miliary form (extremely rate) (Case 2).
b). Reticular form (Case 3).
c). Large Nodular form (Case 4).

The miliary form is extremely rare being described only in those cases with wide spread involvement of parenchymal organs and skeletal system. Since pulmonary involvement of Hodgkin's Disease can mimic practically any disease of the lung, classifications based solely upon pathologic-anatomical features; (26) are of little practical value from a clinical point of view. Other classifications based on the radiologic appearance have been proposed and are described in the literature; for example, Ratkoczy (25), Schinz (30,11,12,20,21,32,37). It is felt that these classifications do not serve to help the clinician or radiologist in categorizing this disease. In contrast, the classification presented in this paper as well as being simple and concise is easily applicable for clinical interpretation.

It is of interest to note several cases of pulmonary Hodgkin's combined with tuberculosis were among our cases. Several other authors have also reported this combination (17).

F. RADIOLOGICAL APPEARANCE OF HODGKIN'S DISEASE ACCORDING TO PATHOLOGIC ANATOMICAL CLASSIFICATION:

I. In those cases of compression or invasion of a bronchus by lymphomatous tissues, the radiological appearance will depend upon the location and degree of the bronchial obstruction.
a). If incomplete, it may act as a check valve mechanism whereby air is accumulated under pressure within the involved lobe or lobe segments resulting in volumen auctum. This is manifested radiologically as an area of hyperillumination. The adjacent anatomical structures may concomittently be pushed aside by the emphysematous portion. Under fluoroscopic examination the mediastinum shifts into the opposite side on expiration (Manges' sign).
b). When the bronchial blocking is complete, the parenchyma supplied by the involved bronchus becomes atelectatic, and is characterized radiologically by a homogenous density associated with reduction in size. The adjacent anatomical structures are pulled toward the affected area; and fluoroscopically the mediastinum moves toward the involved region on inspiration.
c). Tissue break-down due to poor drainage followed by necrosis becomes apparent on X-Ray as an air-fluid level within the diseased area. Pneumonic infiltration is characterized by ill-defined, patchy densities surrounding the lesion.

II. Destruction of the tracheal wall by invasion is very difficult to diagnose by means of X-Ray and can be more readily discovered endoscopically. Perihilar and parenchymal involvement may stimulate bronchogenic carcinoma or an inflammatory process and only clinical or additional radiological signs may suggest Hodgkin's Disease.

III. The radiological appearance of hematogenous or lymphogenous spread in Hodgkin's Disease is non-specific and must be differentiated from miliary tuberculosis, Boeck's sarcoidosis, pulmonary metastasis, lymphangitic carcinomatosis and several other pulmonary lesions. A definite diagnosis can only be obtained by histological examination.

G. OTHER COMPLICATIONS OF PULMONARY HODGKIN'S DISEASE:

Aside from the above mentioned complications of Hodgkin's Disease other sequelae may result in the course of this disease. In advanced cases with lobar atelectasis, cavernous break down may occur; (5,12,18,32) however, the tendency for tissue necrosis is seen more frequently in pulmonary neoplasms, especially after radiation therapy. Spontaneous pneumothorax has been reported as the first manifestation (3). Involvement of the esophagus as well as injury of the phrenic and recurrent nerve are frequent sequelae of destructive intraediastinal growth (2,36). Pleural effusion often accompanies intrathoracic Hodgkin's Disease with efferent lymph channel and pleural involvement. The majority of the sternal lesions are osteolytic, and spread mainly by direct extension from the substernal or mediastinal lymph nodes (5). Chlothorax results from compression or erosion of the thoracic duct.

H. ANALYSIS OF 100 CASES OF HODGKIN'S DISEASE IN REGARD TO PULMONARY INVOLVEMENT:

Analysis was made of 100 cases of Hodgkin's Disease in which chest films were studied in retrospect, to evaluate pulmonary involvement. In all cases, the diagnosis of Hodgkin's Disease has been proven either cyto-histologically or by autopsy. Of these hundred cases, sixty had radiographically suggestive intrapulmonary findings, sometime during their course. Not all of these proved to be involved by Hodgkin's. See Table III.

This study is based on 100 documented cases dating from 1944 to 1961 at the Department of Radiology and Radiotherapy, University of Basel, Switzerland, some of which are still being treated.

TABLE II

Sites of involvement observed on first examination.	% of CASES
1) Generalized in lymph nodes, mediastinum and lung parenchyma	14
2) Mediastinum and/or hilar	16
3) Peripheral lymph nodes	70

TABLE III

Sites of involvement during the further course of Hodgkin's disease.

(A) Of 100 cases those showing radiologically suggestive intrathoracic lesion.	75
(B) Of 100 cases those showing radiologically suggestive intrapulmonary lesions.	60
(C) Those dying with radiologically suggestive intra-pulmonary lesions.	39
(D) Those subjected to autopsy with radiologically suggestive intrapulmonary lesions.	31
(E) Those pathologically proven intrapulmonary lesions.	19

The following Table IV shows the incidence and distribution* of the various forms of pulmonary Hodgkin's Disease according to our classification.

TABLE IV

GROUP	(FROM TABLE III)	DIVISION		
		I.	II.	III.
A	(75 cases)	3	58	29
B	(60 cases)	3	58	29
C	(39 cases)	1	38	21
D	(31 cases)	1	32	16
E	(19 cases)	-	20	7

*

These figures are based on the various radiographic manifestations, and includes patients which presented with more than one form during the course of the disease.

ILLUSTRATIVE CASE REPORTS

From the Medical Record library Basel University, Switzerland.

CASE I.

M.F. a 32 year old laborer complained for the past few years of shortness of breath. Fluroscopic examination in June, 1955, revealed a widening of the superior mediastinum and he was referred to the medical clinic. A large cervical tumor was found, excised and diagnosed as Hodgkin's lymphoma. Blood count: Leucocytes 12,200, Lymphocytes 7%, Eosinophiles 2%, Hb. 89%, E.S.R. 22/51.

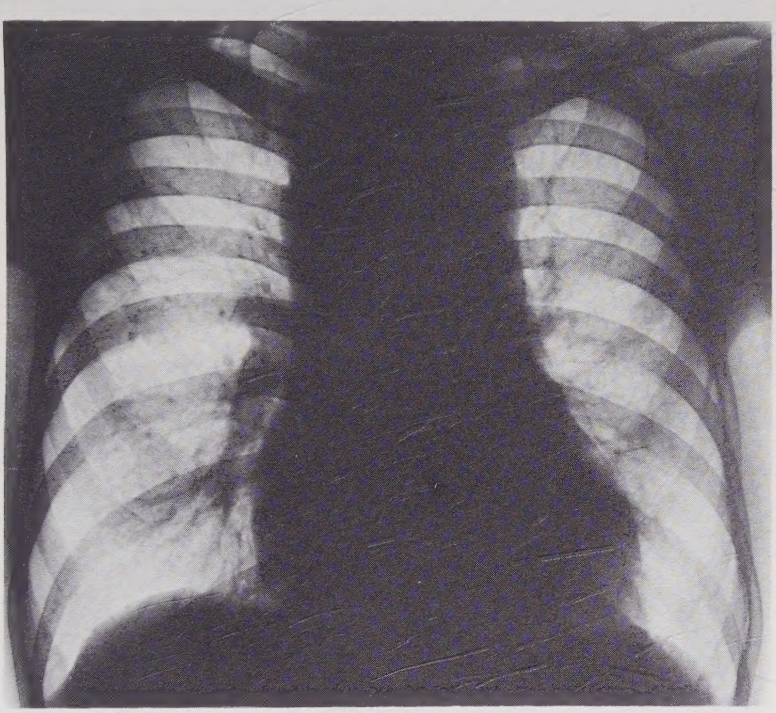

FIG. 1

Examination of the X-Ray taken 11/16/55, (Fig. 1) showed well demarcated polycyclic bulging enlargment of the upper mediastinum to the left and right by tumor masses. There was generalized enlargement of the heart shadow with very small pulsations and a tented density of the left heart border. The lungs were free of pathological structures. On the basis of these X-Ray findings the presumptive diagnosis of mediastinial and pericardial sac involvement with lymphogranulomatosis and pericardial effusion was made. During the period from 11/16 to 12/23, 1955, radiation therapy employing conventional methods was given to dorsal and ventral mediastinum. left and right cervical regions, each receiving 1000 r. This resulted in a complete

remission of the tumor masses and disappearance of the pericardial effusion (Fig. 2) of 12/13/55. In February, 1956, however, a new enlargement of the heart shadow and additional peripheral glandular enlargement (left axilla and cervical) appeared necessitating a second series of radiation therapy following which the patient felt well and was free of symptoms. A follow-up X-Ray taken 2/4/57, (Fig. 3) disclosed an infiltration of the left hilus and the right middle lobe; elevation of the left diaphragm was presumably due to involvement of the phrenic nerve. Paresis of the recurrent nerve was also noted. Further radiation and Dichloren therapy were ineffective. A massive left sided pleural effusion and infiltration of the right middle lobe appeared. (Fig 4) 7/3/57. The extremely cachetic patient finally expired on 1/2/58.

The autopsy showed generalized lymphogranulomatosis. The mediastinum was completely infiltrated and had grown extensively into both lung fields.

This case belongs to category IIc according to the proposed classification displaying infiltrative growth from the mediastinal glands into the lungs and pericardium.

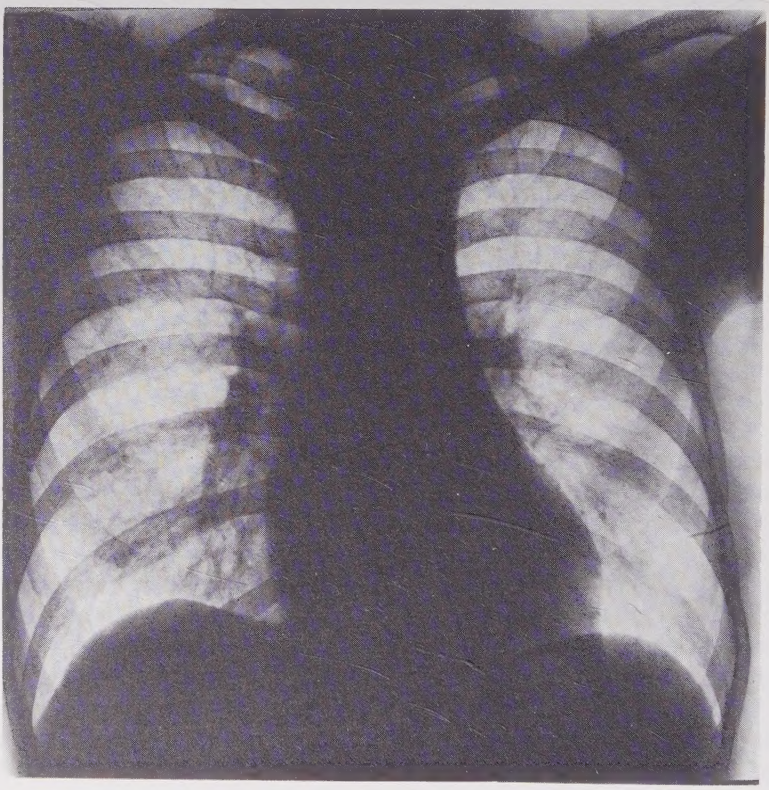

FIG. 2

Fig. 3.

Fig. 4.

CASE 2.

R.H. a 36 year old female was referred for radiation therapy in Jan, 1956, for lymphogranulomatosis which had been diagnosed in December, 1953. Mediastinal and left supraclavicular glands in addition to moderate splenomegaly were present. She had subfebrile temperatures, pruritis and a sedimentation rate of 118/120. Because her symptomatology was already generalized she was started on small doses of radiation (400 to 600 r per field) employing conventional methods. There was practically a complete regression of these enlarged glands following treatment. In the spring of 1957, she developed a large liver tumor and gradually became more cachectic. This tumor regressed markedly following radiation therapy (dosage four fields, 300 r each). The patient recovered and fared relatively well during the following two years although recurrent peripheral lymph node enlargement and enlargement of the spleen and liver necessitated further radiation. During the spring of 1959, however, her general condition rapidly worsened and she developed dyspnea. X-Ray examination on 6/16/59 (Fig.5) showed small dense, patchy dissemination in both lungs beside a few old fibrotic densities in the right apex. During the period from 5/15 to 7/3/59 radiation therapy to the thorax over two dorsal and two ventral fields each totalling 850 r was given on the assumption there had been a hematogenous miliary spread. The infiltrations showed a slight reduction in size following therapy but dyspnea increased and her condition progressively worsened. She expired on 8/20/59 about 6 years after recognition of her illness.

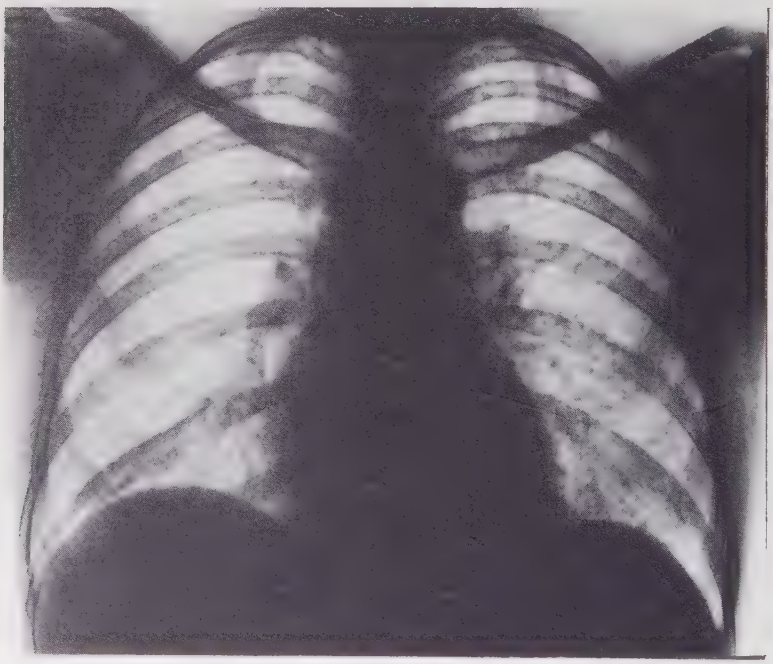

FIG. 5.

The autopsy showed miliary foci of pulmonary lymphogranulomatosis some of which had undergone fibrotic transformation.

This case belongs to category IIIa (Miliary dissemination) according to the proposed classification, a form which is relatively rare.

The onset of the illness was typical. The sensitivity of the liver tumor which developed during the 4th year of illness to radiation therapy is worthy of note.

Case 3.

M.A. A 21 year old laborer with a history of pneumonia in 1954, was treated for myalgia following back pain which occurred after lifting heavy objects. He complained of shortness of breath, anorexia, night sweets and non-productive cough. Hodgkin's disease was diagnosed in the fall of 1955, on the basis of a cervical gland biopsy. Blood count: Leucocytes 10,300, Lymphocytes 70%, Eosinophiles 5%, ESR 9/23. Examination of the X-Ray taken 1/28/56 (Fig. 6) showed an irregular plum-sized protuberance in the right superior mediastinum. The lungs were free of pathological structures and there was no evidence of hepato-splenomegaly. Radiation of dorsal and ventral mediastinum (2000 r each) and 1000 r to the right cervical region resulted in only slight regression of the tumor in the right superior mediastinum.

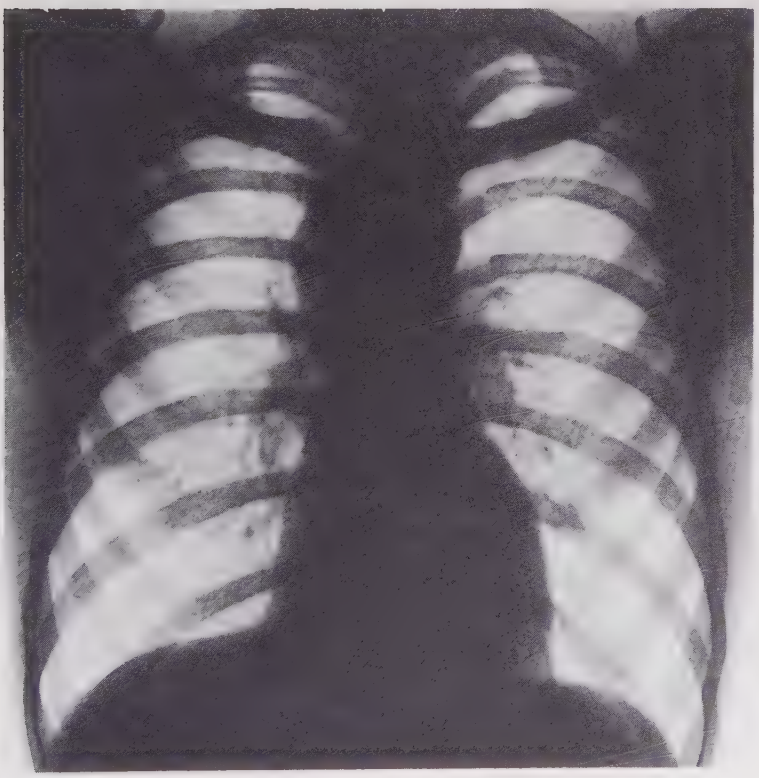

Fig. 6.

In 1956, additional peripheral adenopathy was noted in both axillary and right cervical regions. A good remission was attained with Nitrogen Mustard which was given following an unsuccessful trial to irradicate the tumors with radiation therapy. In the following year, temperature elevations up to 38°c, Leucocytes of 14,000, increased sedimentation rate up to 78/114 accompanied the appearance of bilateral pulmonary involvement (Fig. 7).

Aside from the stationary tumor in the right superior mediastinum and small right sided pleural effusion, thick, streaky, linear densities are seen in both lung bases in addition to a patchy focal dissemination. These foci did not regress following radiation therapy. The patient became progressively cachectic and finally expired 7/7/57.

The autopsy (performed by Professor Werthemann) showed involvement of all organs by Hodgkin's disease. There was lymphangitic spread to both lungs which had extensive infiltrates in addition to a left sided Hydrothorax.

This case falls under classification IIIb which exhibited a reticular type spread of lymphogranulomatosis to the lungs.

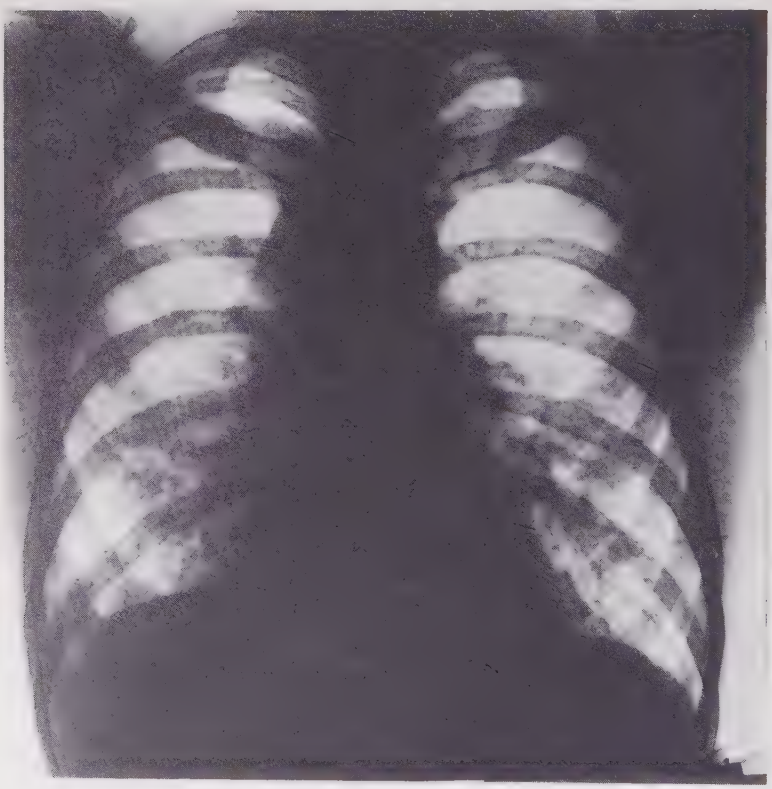

Fig. 7.

Case 4.

A.W. A 37 year old railway worker presented with a history of chronic cough of 3 years duration. In 1956, a mediastinal tumor was found and in 1957, Hodgkin's disease was diagnosed on the basis of a supraclavicular lymph node biopsy.

Examination of the X-Ray taken 2/8/58 (Fig. 8) showed glandular tumors of the superior mediastinum and both hilar regions in addition to a walnut sized infiltration below the left clavicle. Radiation therapy over 3 fields (total dosage of 6000 r) resulted in a complete regression of these foci. The patient was able to continue with his strenuous occupation. A follow-up examination on 10/16/58 revealed an apricot-sized sub-pleural focus in the posterior-basal portion of the right thorax (Fig. 9) which disappeared completely after X-Ray therapy of 2000 r each to the posterior and lateral fields. Four months later an infiltration involving the para hilar region at the base of the right upper lobe accompanied by severe chest pains and moderate splenomegaly were noted. This pulmonary infiltration proved extra-ordinarily resistant to radiation therapy as residual induration in the parahilar fields was present and only partial regression attained. The patient felt well, however, and continued his strenuous occupation. In January, 1961, an egg sized focus was found to the right of the heart (Fig. 10) which regressed after a radiation dose of 1200 r each to an anterior and posterior field.

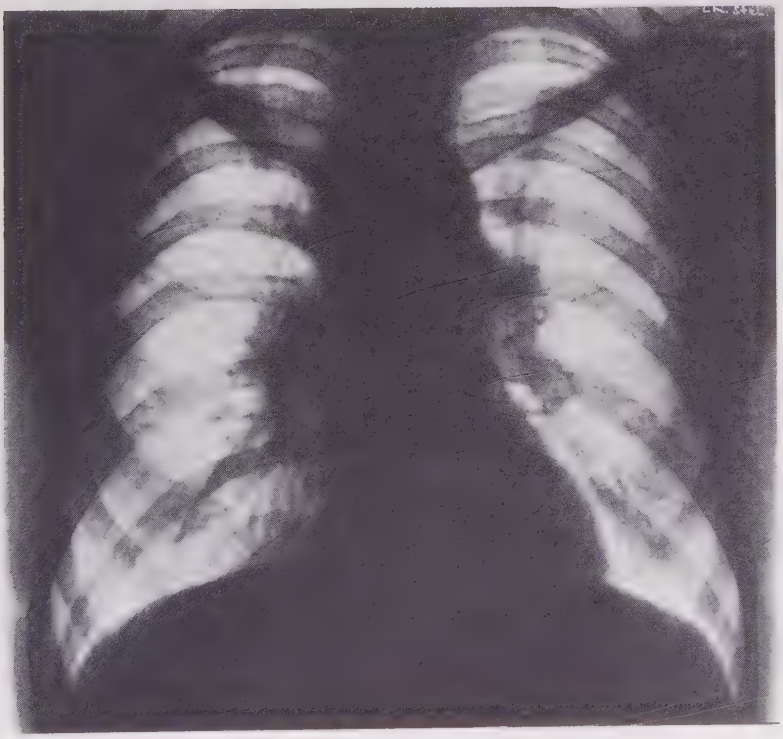

Fig. 8.

At his last visit 12/6/61, a new cherry-sized infiltration was present below the lower pole of the left hilus.

According to the proposed classification this case falls into category IIIc. Five years earlier when the diagnosis of Hodgkin's disease was confirmed, mediastinal glands and intrapulmonary infiltration were already present.

During the course of illness, recurrent pulmonary infiltrations showed prompt regression with radiation therapy except for one which was resistant to radiation and left residual induration.

Fig 9.

Fig 10.

J. COMMENT:

If one surveys the course of intrathoracic Hodgkin's with all its varieties in a large series of cases, the significance of X-Ray findings and interpretation is apparent (28,33,34.) The cervical and mediastinal lymph nodes are frequently the earliest recognizable sites involved with Hodgkin's disease. (5,35.) The importance of Roentgenologic diagnosis in the evaluation of enlarged mediastinal glands is apparent. Involvement of the lungs by Hodgkin's disease is not rare. This spread occurs by infiltrative growth from the mediastinum, spread via lymph channels, or metastasis via hematogenous pathways.

According to Scheinmel (29,31) et. al. involvement of the lung parenchyma is not necessarily an ominous sign in regard to life expectancy. The extent of the disease is a more significant yard stick for assessing the prognosis.

Localized peripheral Hodgkin's Disease as well as intrapulmonary and mediastinal involvement are an indication for radiation therapy; whereas, cytostatica or a combination of these should be reserved for advanced cases. The variable course of the disease necessitates an individual therapeutic approach, and thus hard-and-fast rules cannot be followed (22,24). Even cases have reportedly done well for extended periods of time after surgical extirpation of mediastinal lymph nodes.

Despite the fact that we are unable to effect a cure with the therapeutic measures available to us today, we may often help delay or prevent the intrathoracic complications, and keep patients free of complaints for many months and even years.

K. SUMMARY:

A study of 100 cases of Hodgkin's Disease is made. In 31 autopsies performed, 19 (61%) revealed pulmonary involvement. To demonstrate the variations and frequency of the different forms of pulmonary Hodgkin's Disease, chest X-Rays are presented with a discussion of four cases.

A radiographic classification of pulmonary Hodgkin's based on pathologic anatomical changes has been proposed.

In those cases with predominantly pulmonary manifestations the correct diagnosis is often missed. It is usually difficult to differentiate pulmonary Hodgkin's Disease from tuberculosis, silicosis, pulmonary abscess, sarcoidoisis, metastatic disease, mycotic infections and branchus carcinoma among other lesions. Frequently it is only after biopsy or post mortem examination that one becomes cognizant of the true nature of this disease.

ZUZAMMENFASSUNG:

Von 100 Fällen mit hodgkin'shen Krankheit von welchen 31 seziert worden sind, wiesen 19 davon eine pulmonale Beteiligung auf.

Röntgenbilder mit Diskussion von 4 Fällen sind presantiert als Beispiele der Variationen und Häufigkeit verschiedener Formen.

Eine radiographische Klassifizierung der hodgkin'schen Krankheit, begründet auf pathologish-anatomischen Veränderungen, wurde vorgeschlagen.

Die korrekte Diagnose wird oft übersehen in Fällen von vorwiegenenden pulmonalen Manifestationen. Differential diagnostish ist Sie häufig schwer abzugrenzen, u.a. gegen Tuberkulose, Silikose, Pulmonal-abscesse, Sarkoidosis, isolierte Metastasen, mykotische Infektion und Bronchial carcinome.

Entscheidend ist natürlich eine Biopsie oder die Sektion.

I take this opportunity to thank Dr. K. Meinardus, of the Roentgen Institute, for his guidance and help in classifying the many X-rays.

BIBLIOGRAPHY

1. Alder, A. Und Zbinden, F: Zur therapie Des Lymphogranuloms (Morbus Hodgkin). Schweizerische Gesellschaft fur Inner Medizin, (924,1953)

2. Anacker, H.: Die rontgenologischen Merkmale des Lymphknoteneinburchs in den bronchus. Fortschritte auf dem Gebiete der Rontgenstrahlen (87,588-97,1957.)

3. Baker, C. and Mann, W.N.: Hodgkins Disease, A study of 65 cases: Guys Hospital Rep. (89,83-107,1939.)

4. Berman, L: Malignant Lymphomas their classification and relation to Leukemia, Blood The Journal of Hematology, Vol. VIII No. 3 (195-210,1953.)

5. Bollag, W. und Schwarz, E: Lymphogranulomatose des Mediastinums und der Lunge. Handbuch der Innere Medizin Bd IV/3 Spezielle Teil II, 1956.

6. Bostick, W. L.: Evidence for the Virus etiology of Hodgkins Disease, Ann. New York Acad Sc. Vol. 73, 307-334, 1958.

7. Braun, H. und Bruges, E: Die Isolierte Lungen Lymphogranulomatose, gleichzetig ein Beitrag zur Frage des familiaren Vorkomemmens der Lymphogranulomatose,. Aerztl. Wschr 12 (3), 64, 1957.

8. Carter, J.R.: Some basic concepts regarding tumors of Lymphoid tissue. Am. J. Roentgenology, 76,956-959, 1956.

9. Custer, R.P.: Borderlines dim in malignant disease of the blood forming organs. Radiology 61: 764-770,1953.

10. Custer, R.P. and Bernhard, W.G.: The Interrelationship of Hodgkins Disease and other lymphatic tumors. Am. J.M. Sc. 216: 625-642, 1948.

11. Delarue, J., Mme Verley, J.M., Chomette, G., Abelanet, R. Les Localisations Respiratoires Intrathoracuques de la Maladie de Hodgkin Annales D'Anatomie Pathologique Tom V 5-31, 1960.

12. Ellman, P. and Bowdler, A.J.: Pulmonary manifestations of Hodgkin's Disease. Brit J. Dis. Chest 54, 59-71,1960.

13. - - - - and Friend, C.: The Lymphomas, N.Y. Ann Int. Med., 52, 201-222-, 1960.

14. Gall, E.A.: The cytological identity and interrelation of mesenchymal cells of lymphoid tissue Ann New York Acad. Sc. Vol. 73, 120-130, 1958.

15 Jackson, H. and Parker, F.: Hodgkins Disease and allied disorders, New York Oxford University Press 1947.

16. Kellner, E.: Beziehungen zwischen Morbus Hodgkin and Sarkom, Archiv fur Geschwulstforschung 12, 172-201,1958.

17. Leopold, P.G., Ahlemann, H.R.: Beitrag zur Differentialdiagnose der Verschattung des oberen Mediastinum (unter besondere Berucksichtungung der differentialdiagnostistichen Abgrenzung tuberkulose von der mediastinalen Form einer Lymphogranulomatose. Zschr. Ges Inn Med. 12 (4), 172-7,1957.

18. Lessen W. Van, Seidel, K.: Multiple Kavernenbildung bei Lungen Lymphogranulomatose. Fortsch. auf dem Gebieten der Rontgenstrahlen und Nuklear Medizin, 86, 523-25, 1957.

19. Maximow, A.A., Bloom, W.: A textbook of Histology, 1952.

20. Moolton, S.W.: Hodgkins Disease of the lungs. Am. J. Cancer, 21,253-294, 1934.

21. Nickau, R.H., Reeves, R.J.: Pulmonary manifestations of Hodgkins Disease. Journal of the Florida Medical Association, 44, (11), 1224-6, 1958.

22. Oeser, H. Strahlenbehandlung der Geschwulste. Munchen und Berlin Urban and Schwarzenberg, 1954.

23. Osgood, E.E.: A Unifying concept of the etiology of the Leukemias Lymphomas and cancers. Journal of the National Cancer Institute, 18 (2), 155-166, 1957.

24. Peters, M.W. and Middlemiss, K.C.H.: Study of Hodgkins Disease treated by irradiation. American Journal of Roentgenology, 79, 114-21, 1958.

25. Ratkoczy, W.: Die Pathologie und Therapie der Lymphogranulomatose, Leipzig Georg Thieme, 1940.

26. Rottino, A. and Hoffman, G: The pathology of the Lung in Hodgkins Disease Am. J. of Surgery 89,550-55,1955.

27. Ruttner, J.R.: Zur pathologischer Anatomie der Lymphogranulomatose mit besondere Berucksichtigung ihrer nosolgischen Stellung. Schweiz Ztchr. Allg. Path. 16, 1-48, 1953.

28. Sands, J. Schulz, D.M. and Aromstan, E.M.: The indeterminate pulmonary infiltration: Our diagnostic dilema. A.M.A. Archiv Int. Med. 103 (1) 23-27, 1959.

29. Scheinmel, A. Roswitt, B. and Lawrence, L.R.: Hodgkins Disease of the Lung. Appearance and therapeutic management. Radiology, 54, 15-65, 1950.

30. Schinz, H., Baensch, W., Fried, L. und Uehlinger: Lehrbuch der Rontgen Diagnostik Bd. III/1 Stuttgart: Georg Thieme, 1952.

31. Smetana, H.F. and Cohen, B.M.: Mortality in relation to histologic type in Hodgkins Disease, Blood, The Journal of Hematology, XI, 211-224, 1956.

32. Verse, M.: Die Lymphogranulomatose der Lunge und des Brustfells Handbuch der Speziellen pathologischen Anatomie und Histologie III/3 Berlin J. Springer, 280, 1931.

33. Vieta, J.O. and Craver L.F.: Intrathoracic manifestations of Lymphomatoid diseases. Radiology 37, 138-158, 1941.

34. Voth, H. Zum Ablauf der Thorakalen Lymphogranulomatose. Dtsch Archiv Klin Med. 204, 9, 122-144, 1957.

35. Wessler, H. and Greene, C.M.: Intrathoracic Hodgkins Disease (involvement of Lymphatic collection in the Lungs) Jour. A.M.A. 74, 445-448, 1920.

36. West, W.O. and Bournoncle, B.A.: Spontaneous perforation of the esophagus in Hodgkins Disease, American Journal of Gastorenterology, 33, 335-42, 1960.

37. Wolpaw, S.E., Higley, C.S. and Hauser, H: Intrathoracic Hodgkins Disease American J. of Roentgenology and Radium Therapy, 52, 374-97, 1944.

38. Yardumian, K. and Myers, L: Primary Hodgkins of the Lung, A.M.A. Archives of Int. Medicine 86, 233-44, 1950.